LIQUID DISPENSING SYSTEM

BACKGROUND

[0001] Liquid dispensing systems are used to dispense liquids for various applications. For example, such systems are used to dispense chemicals for performing inorganic, organic, and analytical procedures.

SUMMARY

[0002] Liquid dispensing systems, and methods of dispensing liquids, are provided. A liquid dispensing system according to an exemplary embodiment comprises a pressurized gas supply and a vessel for containing a liquid. The vessel is in fluid communication with the pressurized gas supply, which is operable to pressurize the liquid. A first valve is in fluid communication with the pressurized gas supply and the vessel. A fluid line is in fluid communication with the first valve and with a second valve. The first valve is operable to selectively control flow of the pressurized gas, or the liquid, into the fluid line. An indicator is operably associated with the second valve. The indicator effects closing of the second valve when a predetermined amount of the liquid has been supplied into the fluid line from the vessel.

[0003] In an exemplary embodiment, the indicator comprises a timer operable to effect opening of the second valve for a predetermined amount of time, and closing of the second valve after the predetermined amount of time has elapsed. Liquid is supplied into the fluid line from the vessel for the predetermined amount of time. In another exemplary embodiment, the indicator comprises a weighing device, which measures the weight of the vessel containing the liquid. In still another exemplary embodiment, the indicator comprises a level detector, which monitors the level of the liquid in the vessel.

[0004] In another exemplary embodiment, the liquid dispensing system comprises a solvent supply in fluid communication with the first valve, the fluid line, and the second valve. The solvent supply can be operated to supply at least one solvent into the fluid line to clean and remove the liquid from the fluid line via the second valve.

[0005] The liquid dispensing system can comprise a controller to control selected components of the system.

[0006] The liquid dispensing system can comprise more than one dispensing system to provide the capability of dispensing different liquids for applications, such as chemical reactions.

[0007] An exemplary embodiment of a method of dispensing a liquid comprises supplying pressurized gas into a vessel containing a liquid so as to pressurize the liquid; opening a first valve in fluid communication with the pressurized gas supply and the vessel; operating the first valve to supply the liquid from the vessel into a fluid line in fluid communication with the first valve and with a second valve; determining when a predetermined amount of liquid has been supplied into the fluid line from the vessel; closing the second valve when the predetermined amount of liquid has been supplied into the fluid line; and operating the first valve to supply the pressurized gas into the fluid line to dispense the liquid via the second valve.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] FIG. 1 depicts an exemplary embodiment of the liquid dispensing system including a timer.

[0009] FIG. 2 depicts another exemplary embodiment of the liquid dispensing system including a weighing device.

[0010] FIG. 3 depicts another exemplary embodiment of the liquid dispensing system including a level detector.

[0011] FIG. 4 depicts another exemplary embodiment of the liquid dispensing system including two dispensing systems.

DETAILED DESCRIPTION

[0012] In certain applications, it is desirable to dispense a precise amount of one or more chemicals from a dispensing device. For example, for certain chemical reactions, reactants need to be combined in accurate ratios in order for chemical reactions to occur and produce desired products. Accurate amounts of liquids can be transferred into a reactor using a syringe, for example. However, air-sensitive or oxygen-sensitive chemicals may come into contact with air as they are being transferred. Accordingly, there is a need for a liquid dispensing system that can transfer chemicals without the occurrence of such air contact.

[0013] In addition, liquid dispensing systems used to dispense corrosive chemicals need to be cleaned periodically after use, preferably between each run. Otherwise, components of the systems that are made of materials sensitive to such corrosive chemicals may be degraded by being exposed to the corrosive chemicals for an excessive period of time.

[0014] However, in some liquid dispensing applications, it is not suitable to open certain components of the liquid dispensing system between each run. One such application is the synthesis of radio chemical compounds. In positron emission tomography (PET), radio chemical compounds, also referred to as "radio pharmaceutical compounds," are labeled with positron emitting radio isotopes. These compounds are synthesized using a system including a vessel for the dispensing and mixing of the starting chemicals. Components of the system can be automatically controlled to allow the chemistry to be performed in an isolated location, such as in a shielded hot cell. For example, dispensing, mixing, and heating of the chemicals to produce the radio chemical compounds can be automatically controlled in some systems. However, radio chemical compounds that have a short half-life need to be synthesized frequently. It is undesirable to open certain components (e.g., the hot cell) of the system quickly and frequently,

especially between each run, because an operator may consequently be exposed to radioactive materials.

[0015] In light of the above concerns associated with dispensing certain chemicals, a liquid dispensing system is provided that is capable of delivering chemicals in small amounts. Such chemicals can be, for example, inert, corrosive, air-sensitive, moisture-sensitive, or oxygen-sensitive chemicals. The liquid dispensing system preferably is capable of delivering such chemicals in accurate, repeatable amounts. Accordingly, the liquid dispensing system is useful for dispensing liquids for undergoing chemical reactions that may need such close control.

[0016] In an exemplary embodiment, the liquid dispensing system can be cleaned without having to disassemble the system, and potentially allow certain types of chemicals to escape. The system can be cleaned to remove corrosive chemicals from components of the system that contact the chemicals to avoid prolonged exposure of the components to the chemicals. Consequently, component lifetimes can be extended. Moreover, vessels of the liquid dispensing system that contain the chemicals for synthesis can be filled a single time before operation, preferably under a protective atmosphere, to prevent the chemicals from contacting air, and obviate having to open the vessel for refilling purposes before all runs have been completed.

[0017] FIG. 1 shows an exemplary embodiment of a liquid dispensing system 10. The liquid dispensing system 10 includes a vessel 12 containing a liquid 14. The liquid 14 is dispensed in desired amounts by operation of the liquid dispensing system 10. A gas supply 16 is arranged in fluid communication with the vessel 12 via fluid lines 18, 21. A valve 20 is in fluid communication with the vessel 12 via a fluid line 22. A valve 25 is arranged in fluid communication with the valve 20 via a fluid line 24.

[0018] The valve 20 is preferably a three-way valve. The valve 25 is preferably a two-way valve. However, other valve constructions can be used for the valve 20

and valve 25. An exemplary suitable two-way valve for the liquid dispensing system is Model HP 225 T012 available from Neptune Research Inc., West Caldwell, New Jersey. An exemplary suitable three-way valve is Model HP 225 T032 also available from Neptune Research Inc.

[0019] The liquid dispensing system 10 is capable of dispensing a selected amount of liquid. The amount of liquid can be the same, or it can be different, for different runs of the liquid dispensing system 10. In an exemplary embodiment, the valve 25 can be opened for a desired amount of time to control filling of the fluid line 24, accurately controlling the volume of liquid that can be dispensed from the liquid dispensing system 10 via the fluid line 34. The liquid dispensing system 10 can include any suitable component operably associated with the valve 25 to allow the valve 25 to be opened for a desired amount of time in order to achieve controlled filling of the fluid line 24. Preferably, the liquid dispensing system 10 includes an indicator that is operable to indicate when the valve 25 should be opened and closed to allow for controlled dispensing of liquids by the system.

[0020] In an exemplary embodiment, the indicator is a timer 26 in control communication with the valve 22 via a control line 35. The timer 26 can be selectively set to allow the valve 25 to be opened and then closed after a selected amount of time has elapsed in order to introduce a desired volume of liquid into the fluid line 24 via the valve 20 and the fluid line 22.

[0021] In another exemplary embodiment of the liquid dispensing system 10 shown in FIG. 2, the volume of liquid introduced into the fluid line 24 from the vessel 12 can be controlled by operation of an indicator that monitors the weight of the vessel 12 containing the liquid 14. For example, the indicator can be a weighing device 42 (e.g., a highly accurate balance). The weighing device 42 preferably is arranged in control communication with a controller 28 via a control line 43. The supply of liquid 14 from the vessel into the fluid line 24 can be terminated by closing the valve 25 after the weighing device 42 determines that the weight of the vessel 12 containing the liquid 14 is reduced by a predetermined

amount (i.e., relative to the weight of the vessel 12 at the time at which the valve 25 is opened) that corresponds to a desired dispensed volume of the liquid 14.

[0022] In another exemplary embodiment of the liquid dispensing system 10 shown in FIG. 3, the volume of liquid introduced into the fluid line 24 from the vessel 12 can alternatively be controlled by an indicator that detects the level of the liquid 14 in the vessel 12. For example, the indicator can be a level detector 44, which emits a light beam 46 or the like, which impinges on the surface of the liquid 14. The level detector 44 preferably is arranged in control communication with the controller 28 via a control line 48. The supply of the liquid 14 from the vessel 12 into the fluid line 24 can be terminated by closing the valve 25 when the level detector 44 determines that the level of the liquid 14 in the vessel 12 has been decreased by a predetermined amount (i.e., relative to the level of the liquid in the vessel 12 at the time at which the valve 25 is opened) that corresponds to a desired dispensed volume of the liquid 14.

[0023] The controller 28 is operable to send control signal(s) to components of the liquid dispensing system that are in control communication with the controller 28 to cause the components to function in accordance with the control signals. The controller 28 can be connected to a computer 50, which is operable to produce control signals for the controller 28. The computer 50 can incorporate, or be in communication with, logic embodied in software instructions stored in an accessible memory, digital logic circuit, analog logic circuit, or combination thereof.

[0024] As shown in FIG. 1, the controller 28 preferably is in control communication with the timer 26 via a control line 33. Accordingly, the controller 28 can send control signals to the timer 26 to control the opening and closing of the valve 25

[0025] However, some or all of the components of the liquid dispensing system 10 that are described herein as preferably being controlled by the controller 28 can alternatively be manually operable, e.g., valve 20, as well as other system components, can be manually operable.

[0026] The controller 28 preferably also is in control communication with the gas supply 16 and the valve 20. Accordingly, the controller 28 can control opening of the valve 20 to allow gas to be supplied from the gas supply 16 into the fluid line 24, and liquid 14 to be supplied from the fluid line 22 into the fluid line 24.

[0027] The liquid dispensing system 10 can include an optional solvent supply 30 arranged in fluid communication with the valve 20 via the fluid lines 19, 32. The solvent supply 30 can include, or be in fluid communication with, at least one source of solvents. The solvent supply 30 preferably is in fluid communication with a pressurized gas supply, e.g., an inert gas supply. The solvent supply 30 may supply one or more of acetone, water, NaOH, ether, and the like. More or fewer solvents, different solvents, and mixtures of solvents and inert gas (e.g., nitrogen), can be delivered by the solvent supply 30. The liquid dispensing system 10 can be cleaned with solvent after each dispensing run, or at other desired times, as described in greater detail below.

[0028] The fluid lines of the liquid dispensing system 10 are preferably made of materials that do not react with, or otherwise affect, fluids (liquids or gases) that are flowed through the fluid lines during operation of the liquid dispensing system. Based upon the selection of fluids that are to be flowed through the fluid lines, materials suitable for use with those fluids can be used for the fluid lines. For example, the fluid lines can be made of non-metallic materials, such as polytetrafluoroethylene (PETFE), PEEK, and the like, as well as of metals, such as stainless steels, and the like.

[0029] The cross-sectional flow area and fluid volume of the fluid lines of the liquid dispensing system 10 can be varied depending on various factors including the particular liquids to be dispensed. The fluid lines can have the same volume, or they can have different volumes, from each other. The fluid line 24 preferably has a sufficient volume to contain the largest volume of liquid that is desired to be dispensed by the liquid dispensing system. For example, the liquid dispensing system 10 can be constructed to dispense a volume of from about 100 μl to about 1

ml. In an exemplary embodiment, the fluid line 24 can have a volume of about 1.2 ml.

[0030] The fluid line 24 can be at room temperature. Alternatively, the liquid dispensing system 10 can include suitable heating and/or cooling capabilities to heat and/or cool the fluid line 24 to desired temperatures above and/or below room temperature.

[0031] The liquid dispensing system 10 can provide accurate dispensing of various liquids. For example, the liquid dispensing system can dispense small amounts of liquid with an accuracy of from about 1 to about 2% of the total volume of the fluid line 24 in a repeatable manner. Preferably, the dispensing is not affected by the presence of dead volume in the fluid line 22. The dead volume of the fluid line 22 between the vessel 12 and the valve 20 can be filled with liquid during the first filling run of the liquid dispensing system 10. Once the fluid line 22 is filled with liquid, it remains completely filled. Consequently, for subsequent liquid dispensing runs, there is no time delay from the time of opening of the valves 20 and 25 until liquid begins to enter the fluid line 24. After the fluid line 24 contains the desired volume of liquid, the valve 25 is closed. The valve 25 preferably is closed in response to a control signal from the timer 26, or other indicator. The valve 20 can then be opened to gas pressure via fluid line 19. The entire volume of the liquid contained in the fluid line 24 can be transferred through the fluid line 24 and the fluid line 34 when the valve 25 is re-opened.

[0032] The liquid dispensing system 10 can include an optional valve 17 to provide for selective switching capabilities between the supply of pressurized gas from the gas supply 16 via fluid lines 19, 21, and the supply of solvent from the solvent supply 30, via the fluid lines 19, 32. The valve 17 can be a two-way valve, a three-way valve, or other valve construction. The liquid dispensing system 10 can be cleaned all the way through the fluid line 34, e.g., up to a vessel into which liquid is dispensed. The liquid dispensing system 10 allows for repetitive use, including for dispensing applications that may need the system to be completely

cleaned between runs (e.g., applications that may involve two or more reaction steps using chemicals that are incompatible with each other). The cleaning can remove corrosive chemicals from the liquid dispensing system 10, and thereby extend the lifetime of components that are sensitive to such chemicals.

[0033] The provision of the fluid line 32 and the valve 17 also allows solvent to be flowed from the solvent supply 30 into the vessel 12 via the fluid line 18. The liquid dispensing system 10 is operable to clean and empty the vessel 12 when the dispensing runs have been completed.

[0034] The liquid dispensing system 10 can be operated to deliver a variable volume of liquid, particularly without having to physically reconfigure the system (e.g., replace one or more fluid lines with fluid lines having a different volume). That is, different runs of the liquid dispensing system 10 can dispense different desired volumes of the liquid 14 contained in the vessel 12. For example, a calibration curve that relates dispensing time (e.g., the amount of time that valve 25 is opened to allow liquid to be flowed into the fluid line 24) to the dispensed volume (e.g., the amount of liquid that is flowed into the fluid line 24 during the time that the valve 25 is opened) can be predetermined. The liquid dispensing system 10 can be calibrated for each different chemical that is dispensed. As some liquids are highly compressible (e.g., THF), calibration curves for each liquid are preferably provided.

[0035] The liquid dispensing system 10 can be operated in the following manner. Valves 20 and 25 are opened for a sufficient amount of time to fill the dead volume between the vessel 12 and the valve 20. By filling the dead volume, an unknown volume of gas in the fluid line 22 between the vessel 12 and the valve 20 is eliminated. Subsequent dispensings of the liquid can be performed in the manner described above. Once there is no dead volume of gas in the fluid line 22 between the vessel 12 and the valve 20, each subsequent dispensing of liquid is accurate. Assuming that the pressure and the timing for the opening of valve 25 are maintained constant, the liquid dispensing system 10 can be operated to dispense a

constant volume of liquid via the fluid line 34. The liquid dispensed through the fluid line 34 can be introduced into a vessel (e.g., a reactor, a storage container, or the like), deposited onto a stationary or moving surface, or the like.

[0036] An exemplary operating sequence for the dispensing of liquid by the liquid dispensing system 10 is as follows. The vessel 12 is pressurized at a constant pressure. The pressure is preferably between 0 and 30 psi, and more preferably between 5 and 15 psi. To transfer liquid between the valve 20 and the valve 25 via the fluid line 24, a selected time value is entered in the timer 26. The selected time value is preferably based on a predetermined relationship between the volume of liquid dispensed by the liquid dispensing system 10 and the time value at a selected delivery pressure for the liquid. The relationship between the volume of liquid dispensed and the time value can be provided in any suitable form, such as in graphical form. The valve 25 is opened, which starts the countdown of the timer 26. When the timer 26 countdown ends, the valve 25 is closed automatically under control of the controller 28, and the transfer of liquid via the fluid line 24 is stopped. The valve 20 is then actuated to allow pressurized gas to be supplied from the gas supply 16 into the fluid line 24. The valve 25 is opened and liquid is flushed by the pressurized gas from the fluid line 24 out of the liquid dispensing system via the fluid line 34.

[0037] In order to clean the liquid dispensing system 10 after a dispensing run is completed, the valve 17 can be actuated to allow solvent to be supplied from the solvent supply 30 via the fluid lines 19, 32 into the fluid line 24.

[0038] FIG. 4 shows a liquid dispensing system 100 according to another exemplary embodiment. The liquid dispensing system 100 preferably includes a controller (not shown) for controlling components of the system. The liquid dispensing system 100 includes two separate systems, each including a vessel 112 containing a liquid 114 to be dispensed, a valve 120 in fluid communication with the vessel 112 via a fluid line 122, a valve 125 in fluid communication with the valve 120 via a fluid line 124, and a fluid line 134 in fluid communication with a

vessel 140. A timer 126 is in communication with each valve 125. The vessel 140 can be, for example, a reactor. The liquids in the vessels 112 are typically different from each other. The liquid dispensing system 100 can include more than two such systems to dispense more than two different liquids into the vessel 140.

[0039] A gas supply 116 and an optional valve 117 are in fluid communication with the valves 120 via fluid lines 119, 162 to allow pressurized gas to be supplied to the fluid lines 124.

[0040] The liquid dispensing system 100 can optionally include a solvent supply 130 arranged in fluid communication with a solvent selector 150 via a fluid line 152, a valve 154 in fluid communication with the solvent selector 150 via a fluid line 156, and a fluid line 158 in fluid communication with the valve 154 and the valve 117.

[0041] The liquid dispensing system 100 can also include other optional components, such as a gas supply 168 in fluid communication with a valve 174. The valve 174 is optionally in fluid communication with a pressure sensor or pressure regulator 170 via a fluid line 172. A fluid line 175 connects the solvent supply 130 and the pressure sensor or pressure regulator 170.

[0042] The solvent supply 130 preferably is operable to selectively supply solvent to the fluid lines 124 simultaneously, or to supply solvent to one fluid line 124 while not supplying solvent to the other fluid line 124.

[0043] The liquid dispensing system 100 can optionally also include a recovery vessel 180 in fluid communication with the vessel 140 via fluid lines 184 and 186. For example, products produced in the vessel 140 can be transferred to the recovery vessel 180. A valve 182 controls fluid flow into the recovery vessel 180.

[0044] The liquid dispensing system 100 can optionally also include a waste vessel 190 in fluid communication with the vessel 140 via fluid lines 194, 196 and 186, and valves 192 and 198. Gas and/or liquid waste can transferred into the waste vessel 190.

[0045] The liquid dispensing system can be used for various liquid dispensing applications and for dispensing various liquids. In chemical applications, the liquid dispensing system can be used in analytical, organic, and inorganic procedures. The liquid dispensing system is particularly suitable for use in organic radiochemistry applications, such as the synthesis of ^{11}C and ^{18}F radio chemical compounds, e.g., ^{11}C methyl iodide synthesis. In such applications, the liquid dispensing system can dispense accurate amounts of liquids in a repeatable manner. In addition, the liquid dispensing system can be cleaned without having to disassemble its components, which reduces the possibility of operator exposure to radioactivity.

[0046] The liquid dispensing system can be used to perform chemical synthesis in the following exemplary manner.

Example:

[0047] Methyl iodide can be synthesized according to the following procedure using the liquid dispensing system 100 shown in FIG. 4. Under an inert atmosphere, one vessel 114 containing lithium aluminum hydride ($LiAlH_4$) in solution in tetrahydrofurane is loaded on the liquid dispensing system. The other vessel 114 containing hydriodic acid solution is loaded on the liquid dispensing system. The liquid dispensing system is operated to dispense the lithium aluminum hydride solution into the reactor 140. The dispensed volume of the lithium aluminum hydride solution can be, for example, from about 1 μl to about 1 ml, preferably from about 50 μl to about 300 μl. Using a suitable trap and release system for $^{11}CO_2$, the trapped $^{11}CO_2$ is supplied to the reactor 140 to react with the lithium aluminum hydride solution. After solvent evaporation, the other dispensing system of the liquid dispensing system 100 is operated to dispense the hydriodic acid solution into the reactor 140. The dispensed volume of the hydriodic acid solution can be from about 1 μl to about 1 ml, preferably from about 50 μl and 500 μl. Using a suitable heater, the mixture can be distilled to provide ^{11}C-methyl

iodide. After the synthesis, the liquid dispensing system 100 is completely cleaned using one or more solvents supplied from the solvent supply 130.

[0048] While the invention has been described in detail with reference to preferred embodiments thereof, it will be apparent to one skilled in the art that various changes can be made, and equivalents employed, without departing from the scope of the invention. Each of the aforementioned documents is incorporated by reference herein in its entirety.